

Research article

## Assessment of diffuse Lewy body disease by 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography (FDG PET)

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Published: 20 February 2003

Received: 19 December 2002

*BMC Nuclear Medicine* 2003, **3**:1

Accepted: 20 February 2003

This article is available from: <http://www.biomedcentral.com/1471-2385/3/1>

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### Abstract

**Background:** Lewy body disease is, after Alzheimer's disease, the second most common cause of senile degenerative dementia with progressive cognitive deterioration, fluctuation of cognitive and motoric functions and psychotic symptoms. It is characterized histologically by the occurrence of Lewy bodies in allocortical, neocortical and subcortical structures. The aim of this study was to measure the cortical glucose metabolism using FDG PET (2-[18F]fluoro-2-deoxy-D-glucose position emission tomography) compared to normal subjects.

**Patients and Methods:** Five patients (5 m, mean age 75 y) with clinically suspected diffuse Lewy body disease (DLB) were studied with FDG PET. PET studies of the head were performed with a Siemens ECAT-ART PET-scanner with attenuation correction using 137-Cs point sources.

**Results:** We found the same distribution pattern of diffuse glucose hypometabolism in the entire cortical region with relative sparing of the primary sensory-motor cortex in all the patients. The few cases reported in the literature so far describe findings similar to ours.

**Conclusion:** The pattern of diffuse glucose hypometabolism in the entire cortex including the occipital region seems to be a typical feature of DLB that is distinctive from dementia of Alzheimer's disease.

### Background

Dementia with Lewy bodies (DLB) has been established as the second most common senile degenerative dementia after Alzheimer's disease (AD) [1–3]. Lewy bodies, first described in 1912 by F.H. Lewy are distinctive neuronal inclusions that may be seen in several different neurodegenerative processes [4]. Lewy bodies are eosinophilic structures located within the cytoplasm of neurons. They are characteristically circular with a dense protein core sur-

rounded by a peripheral halo. They are thought to be the result of altered neurofilament metabolism and/or transport due to neuronal damage and subsequent degeneration, causing an accumulation of altered cytoskeletal elements. 5–10% of asymptomatic individuals have presumably insignificant numbers of Lewy bodies, usually located in the substantia nigra. [5]. Diagnostic criteria for DLB have been defined to allow clinical diagnosis [3]. Until quite recently, post mortem examination provided the

definitive diagnosis. However, while these clinical criteria have high specificity (90–97%), they have low sensitivity (22–75%) [6]. The central clinical feature required for a diagnosis of DLB is a progressive and fluctuating cognitive decline with recurrent visual hallucinations, systematized delusions and spontaneous parkinsonian symptoms. Repeated falls, syncope, transient loss of consciousness and neuroleptic sensitivity are also clinically characteristic. In AD, in contrast, the progressive decline of memory is prominent and neuropsychiatric features usually occur in the later stages [7]. Moderate parkinsonian signs can be observed during both AD and DLB evolution [8]. Thus, in some cases, the clinical distinction of patients with DLB from those with AD may be difficult because of overlapping symptoms such as cognitive decline, psychiatric signs and parkinsonism. When the initial presentation of DLB is characterized by impaired cognition, the disease can mimic AD [5,9].

Differentiation of the two diseases from each other can be achieved by neuropsychological evaluation, which can disclose impaired performance of similar severity in both diseases with regard to attention, frontal lobe function and motor sequencing in DLB and AD [10]. In practice, differential diagnosis by the use of this method is most likely to be realized in specialized centers of neurology and psychiatry. A previous study has shown that noninvasive imaging modalities such as PET or SPECT may be useful methods for the diagnosis of dementing disorders, especially in the differential diagnosis of dementia and depression of the elderly [11]. In another study, it was found that in depression, symmetrically metabolic changes are found in the prefrontal cortex, and these changes improve with treatment [12], which was not typical for dementia.

In AD, the abnormal pattern of regional cerebral blood flow (rCBF) that is characteristic of the disease is bilaterally decreased perfusion in the temporal and parietal regions [13]. However, heterogeneous patterns of rCBF deficits have been seen in AD on examination with SPECT. This heterogeneity may reflect either different stages of the disease or cognitive subtypes [14]. In DLB, temporoparietal hypoperfusion has been shown to be associated with occipital hypoperfusion, which could explain the visual hallucinations in this illness [15].

The aim of this study was to evaluate FDG-PET brain imaging in assessing clinically manifested DLB by measuring regional glucose metabolism.

## Methods

Five patients (5 males, mean age 75 y, age range 69–79) with fulfilled clinical criteria for DLB were referred to our department for PET examination. The disease duration

was  $3 \pm 1$  y. Every patient underwent a psychological examination including MMSE (mini mental state examination). Magnetic resonance imaging (MRI) of the brain was performed in all the patients. The data gathered from the patients were compared to the PET brain images from a normal data base in our department (six normal subjects, 2 males, 4 females, mean age 63, age range 45–79). The normal subjects had no history of neurological or psychiatric disease. The PET images were obtained 30 minutes after i.v. injection of 150 MBq FDG using a Siemens ECAT-ART (CTI, Knoxville, TN, USA). Attenuation correction of the images was made with an additional transmission scan using two  $^{137}\text{Cs}$  point sources [16]. Reconstruction was performed using the filtered back projection method (FBP) applying a Gaussian filter (FWHM 4.0 mm) and a zoom factor of 2.50. An acquisition matrix size of  $128 \times 128$  was chosen. Six regions of interest (ROI) were drawn on a 10 mm thick transaxial brain slice at 4.5 cm parallel to the cantomeatal line (CML) and two ROIs in the central region, and the SUVs of these regions were measured. Z scores for each patient were calculated according to the formula of Albin et al [17], as follows:

$$Z \text{ score} = (\text{patient regional SUV} - \text{controls regional SUV (mean value)}) / \text{controls regional SUV standard deviation}.$$

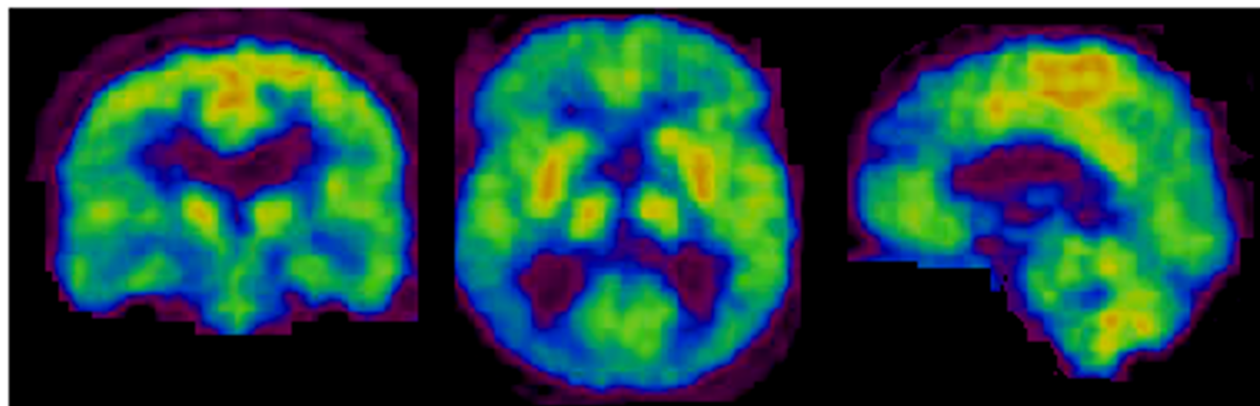
A Z score of  $\leq -2$  was considered to be significant.

## Results

Diffuse reduced glucose uptake in the entire cortical region with relative sparing of the central region (Figure 1), but including the occipital cortex was determined in all the patients, which was less remarkable in patient 2. The mean SUV in the patient group was  $3.30 \pm 0.30$  vs.  $6.10 \pm 0.70$  in the normal subjects. The detailed Z-scores of the patients' cerebral metabolic patterns are shown in Table 1. MRI of the brain showed a mild degree of cortical atrophy in three of the patients without further specific pathologic findings.

## Discussion

Postmortem examination remains the only way to definitively confirm the diagnosis of DLB, which is based on evidence of Lewy bodies in the cortex, the subcortical regions (nucleus basalis of Meynert) and the brain stem (substantia nigra and locus coeruleus) [5,18,19]. With the promise of neuroprotective treatments, early diagnosis is increasingly important. A more extensive cholinergic deficit has been observed in DLB compared with AD [9]. This observation explains the beneficial effects of cholinergic therapy in DLB (cholinesterase inhibitor), which has been shown to improve impaired cognitive functions [20]. This implies that early diagnosis would greatly improve the effectiveness of the treatment.



**Figure 1**  
m, 75 y, Brain FDG-PET shows a diffuse glucose hypometabolism with relative sparing of the central region

**Table 1: Z scores of patient regional mean SUV compared to controls**

Patient Nr.	r.fr.	l.fr.	r.tp.	l.tp.	r.oc.	l.oc.	r.c.	l.c.
P1	-2.7	-3.1	-3.1	-3.4	-3.0	-3.1	-1.4	-2.3
P2	-1.8	-2.1	-2.3	-2.0	-2.9	-3.1	-1.4	-0.6
P3	-2.9	-3.2	-2.6	-3.4	-2.6	-2.9	-1.8	-1.9
P4	-2.3	-2.7	-2.3	-3.1	-2.3	-2.7	-1.9	-1.7
P5	-2.6	-3.0	-2.7	-3.5	-2.7	-3.1	-2.2	-2.1

r. = right, l. = left, fr. = frontal, tp. = temporoparietal, oc. = occipital, c. = central

Although clinical criteria have been defined for DLB [3], development of objective measures to confirm clinical findings would be helpful in clinical routine. Recent studies have suggested that functional imaging with dopaminergic presynaptic ligands and postsynaptic D<sub>2</sub> receptors like <sup>123</sup>I-FP-CIT and <sup>123</sup>I-iodobenzamide help to distinguish DLB from AD, since there are loss of dopaminergic neurons in DLB [21–23]. Another study demonstrated reduced vesicular monoamine transporter type 2 expression in patients with DLB indicating degeneration of nigrostriatal projections [24]. The patients described in this report fulfilled the clinical criteria for DLB. The PET examination revealed that all patients had glucose hypometabolism in the entire cortex with relative sparing of the primary sensory-motor cortex. In addition there was marked hypometabolism in the occipital cortex, which corresponds with results from other studies [1,25]. This characteristic pattern of cortical hypometabolism includ-

ing the occipital areas could be a result of diaschisis due to disruption of intracortical connections. Diaschisis is defined as depression of regional neuronal metabolism and cerebral blood flow caused by dysfunction in anatomically separate but functionally related neuronal regions [26].

The results in this study were obtained in routine hospital work. We did not measure the arterial input function, as performed by Albin et al, since we consider it too invasive and inconvenient to the patient for routine use.

## Conclusion

With the limitation that occipital hypometabolism may be manifested not only in DLB [27], we propose the use of a combination of FDG-PET and striatal dopamine terminal imaging as a supplement to the clinical examination to establish the final diagnosis of DLB and as the basis for a differentiated therapy.

## Competition interests

None declared.

## Authors' contribution

SM designed the study, performed the statistical analysis and drafted the manuscript.

PK performed the quality control of the examination procedure.

HK participated in the design of the study.

TB participated in the design of the study and preparation of the manuscript.

All authors read and approved the final manuscript.

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## Pre-publication history

The pre-publication history for this paper can be accessed here:

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